| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/573,133 | DORFF ET AL. | |
| | Examiner | Art Unit | |
| | Rita J. Desai | 1625 | |

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date. *8/22/06*
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *2/9/10*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

## DETAILED ACTION

### *Election/Restrictions*

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-11, drawn to compounds of formula I wherein Ar is a phenyl or a pyridine.

Group II, claim(s) 12-15, drawn to and treatment of various disorders and kits wherein Ar is a phenyl or a pyridine..

Group III, claim(s) 1-11, drawn to compounds of formula I wherein Ar is other than in group I, A further election of a single disclosed species is required .

Group IV, claim(s) 12-15, drawn to a method of treating various disorders limited to the scope of group III.
The inventions listed as Groups I,III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:
(f) •Markush Practice.• The situation involving the so-called •Markush practice• wherein a single claim defines alternatives (chemical or non-chemical) is also governed by Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.
(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:
(A) all alternatives have a common property or activity, and
(B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or
(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.
(ii) In paragraph (f)(i)(B)(1), above, the words •significant structural element is shared by all of the alternatives• refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common

only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of the existing prior art. The structural element may be a single component or a combination of individual components linked to-gether.
The different Ar substituents have so many variables with the heterocyclic and non-hetero groupings , they have different bonding and properties , and have achieved a different status in the art , and is burdensome to search and hence are objected to as being drawn to an improper Markush group on the grounds of lack of a common nucleus. The term Ar, are so broad in scope that a prior art reference anticipating the claims with respect to one member under 35 USC 102(b) would not render obvious the same claims under 35 USC 103a with respect to another member.

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See EP 1213291.( cited on the 1449)

During a telephone conversation with Mr. Kenneth Mitchell on 2/9/10 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-11 drawn to compounds and composition wherein Ar is a phenyl or a pyridyl. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12-15 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected

process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

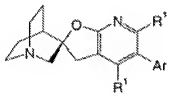
### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over US7238715, Tracy et al.

Applicants claims a re drawn to compounds of the formula

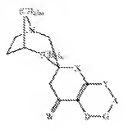


I

formula II:

II

Scope & Content of Prior Art MPEP 2141.01

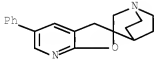


wherein:
m is 1 or 2,
n is 0 or 1,
Y is CH, N or $NO_2$,
X is oxygen or sulfur,
W is oxygen, $H_2$ or $F_2$,
A is N or $CR^2$,
G is N or $CR^3$,
D is N or $CR^4$,
with the proviso that no more than one of A, G and D is nitrogen but at least one of Y, A, G and D is nitrogen or $NO_2$,
$R^1$ is hydrogen or $C_1$-$C_4$ alkyl,
$R^2$, $R^3$ and $R^4$ are independently hydrogen, halogen, $C_1$-$C_4$ alkyl, $C_2$-$C_4$ alkenyl, $C_2$-$C_4$ alkynyl, aryl, heteroaryl, OR, $OC_1$-$C_4$ alkyl, $CO_2R_x$, —CN, —$NO_2$, —$NR_xR_x$, —$CF_3$ or —$OSO_2CF_3$, or $R^2$ and $R^3$, $R^3$ and $R^4$ respectively, may together form a methylene group,

US'715 teaches the same compounds see

See the compound of claim 12 ,

Spiro[1-azabicyclo[2.2.2]octane-3,2'(3'H)-furo[2,3-b]pyridine], 5'-phenyl- (CA INDEX NAME)



Difference between Prior Art and the claims MPEP 2141.02

The difference between the prior art and applicants claim is that applicants claim has atleast one radiolabeled atom tritium or halogen atom.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

All naturally occurring elements have a certain % of the heavier isotope.

So 1) the prior art compounds inherently would have the tritium isotope in the compounds.

2) On page 2 of applicants specifications, they clearly cite several documents which refer to labeled isotopes used for different kinds of studies.

"Goodman, M. M. Clinical Positron Emission Tomography, Mosby Yearbook, 1992, K. F. Hubner et al., Chapter 14. For most biological targets, few isotopes are suitable. The carbon isotope, llC, has been used for PET, but its short half-life of 20.5 minutes limits its usefulness to compounds that can be synthesized and purified quickly, and to facilities that are proximate to a cyclotron where the precursor I:C starting material is generated. Other more energetic isotopes have even shorter half-lives, 13N has a half-life of 10 minutes and :50 has a half-life of two minutes. Nevertheless, PET studies have been carried out with these isotopes as described by Hubner, K. F., in Clinical Positron Emission Tomography, Mosby Year Book, 1992, K. F. Hubner, et al., Chapter 2. [:sF]-labeled compounds have been used in PET studies, but their use is limited by the 110-minute half-life of the isotope. Most notably, [:sF]-fluorodeoxyglucose has been widely used in studies of glucose metabolism and localization of glucose uptake associated with brain activity. [:SF]-L- fluorodopa and other dopamine receptor analogs have also been used in mapping dopamine receptor distribution.

SPECT imaging employs isotope tracers that emit high energy photons (T-emitters). The range of useful isotopes is greater than for PET, but SPECT provides lower three-dimensional resolution. Nevertheless, SPECT is widely used to obtain clinically significant information about analogue binding, localization and clearance rates. A isotope used for SPECT imaging is 123I, a T-emitter with a 13.3 hour half life. Compounds labeled with lz3I can be shipped up to about 1000 miles from the manufacturing site, or the isotope itself can be transported for on-site synthesis. Eighty-five percent of the isotope's emissions are 159 KeV photons, which is readily measured by SPECT instrumentation currently in use.

Increasingly, the precise location and distribution of receptors in the brain and other tissues is of interest to clinical researchers, clinicians and diagnosticians. The distribution of nAChR's in the brains of individuals having disorders involving reduced cholinergic function such as Alzheimer's disease, cognitive or attention disorders, anxiety, depression, smoking cessation, neuroprotection, schizophrenia, analgesia, Tourette's syndrome, and Parkinson's disease is of growing interest ~ the molecular bases of these conditions is being discovered. The precise location and distribution of nAChRs in the brain and other tissues is also of importance in assessing the relevance of animal models of these conditions. "

The above rejection can also be made further in view of Rogers et al Rogers et al. (US2004/0157878A1).

Rogers discloses using the radiolabeled compounds as
See page 1 of the spec.
On page 1 of the specification it teaches these radiolabeled compounds for the study

"Compounds of the present invention are radiolabeled
alpha 7 agonists that are useful as imaging agents and biomarkers for medical therapy
and diagnosis. Such radiolabeled compounds are also useful as pharmacological tools
for studying nAChR function and activity. Accordingly, the invention also provides a
radiolabeled compound of the present invention, or a salt thereof. "

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

Tracy et al teach the compounds with the same use.
Roger et al teaches the radiolabeled compounds useful as imagine agents and biomarkers,
Motivating a person of skill in the art of drug design and discovery such as the applicant to make the radiolabeled compounds .

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

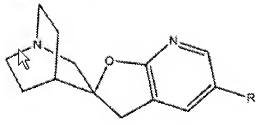
Claims 1-11 are provisionally rejected on the ground of nonstatutory obviousness-type

double patenting as being unpatentable over claim 12, 19 of copending Application No.

12/321951 . Although the conflicting claims are not identical, they are not patentably distinct from each other because these compounds are also drawn to compounds with the same core having a radiolabled substitutent.

See claim 12 wherein R is a phenyl or a pyridyl.

12. (Original) The compound of claim 11, wherein the compound has a structure according to Formula IVa



IVa

wherein

and see claim 19

19. (Original) The compound of claim 11, wherein R comprises one or more radioisotope suitable for use in radiation therapy.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

Claims 1-11 are rejected.

Claims 12-15 are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

February 10, 2010.